



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: **Yu, et al.**

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Title: **Methods of Treatment of Immune System Related Disorders Using Neutrokinin-alpha (as amended)**

Atty. Docket No. PF343P3C4

CLEAN VERSION OF ENTIRE SET OF PENDING CLAIMS

89. (Once Amended) A method of treating an immunodeficiency comprising administering to an individual, a therapeutically effective amount of a protein comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;

(b) the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and

(c) the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

wherein the polypeptide having said amino acid sequence modulates lymphocyte proliferation, differentiation, or survival.

90. (New) The method of claim 89 wherein the protein comprises amino acid sequence (a).

91. (New) The method of claim 89 wherein the protein comprises amino acid sequence (b).

92. (New) The method of claim 89 wherein the protein comprises amino acid sequence (c).

93. (New) The method of claim 89 wherein the protein also comprises a heterologous amino acid sequence.

94 (New) The method of claim 93 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

95. (New) The method of claim 89 wherein said protein is labeled.

98. (Once Amended) A method of treating an immunodeficiency comprising administering to an individual, a therapeutically effective amount of a protein comprising a first amino acid sequence that is 95% or more identical to a second amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;

(b) the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and

(c) the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

wherein the polypeptide having said first amino acid sequence modulates lymphocyte proliferation, differentiation, or survival.

99. (New) The method of claim 98 wherein the protein comprises amino acid sequence (a).

100. (New) The method of claim 98 wherein the protein comprises amino acid sequence (b).

101. (New) The method of claim 98 wherein the protein comprises amino acid sequence (c).

102. (New) The method of claim 98 wherein the protein also comprises a heterologous amino acid sequence.

103. (New) The method of claim 102 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

104. (New) The method of claim 98 wherein said protein is labeled.

107. (New) A method of treating an immunodeficiency comprising administering to an individual, a therapeutically effective amount of a protein consisting of the amino acid sequence of amino acid residues 134-285 of SEQ ID NO:2.

108. (New) The method of claim 107 wherein the protein is fused to a heterologous amino acid sequence.

109. (New) The method of claim 108 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

110. (New) The method of claim 98 wherein said protein is labeled.

113. (Once Amended) A method of treating an immunodeficiency comprising administering to an individual, a therapeutically effective amount of a protein comprising the amino acid sequence of amino acid residues 134-285 of SEQ ID NO:2.

114. (New) The method of claim 113 wherein the protein also comprises a heterologous amino acid sequence.

115. (New) The method of claim 114 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

116. (New) The method of claim 113 wherein said protein is labeled.

119. (Once Amended) The method of claim 113 wherein the immunodeficiency is common variable immunodeficiency (CVID).

121. (Once Amended) The method of claim 113 wherein the immunodeficiency is Selective IgA deficiency.

126. (Once Amended) A method of treating an immunodeficiency comprising administering to an individual, a therapeutically effective amount of a protein consisting of a first amino acid sequence which is 90% or more identical to a second amino acid sequence consisting of amino acid residues 134-285 of SEQ ID NO:2, wherein the polypeptide having said first amino acid sequence modulates lymphocyte proliferation, differentiation, or survival.

127. (New) The method of claim 126 wherein the protein consists of a first amino acid sequence which is 95% or more identical to said second amino acid sequence.

128. (New) The method of claim 126 wherein the protein is fused to a heterologous amino acid sequence.

129. (New) The method of claim 128 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

130. (New) The method of claim 126 wherein said protein is labeled.

133. (Once Amended) The method of claim 126 wherein the immunodeficiency is common variable immunodeficiency (CVID).

135. (Once Amended) The method of claim 126 wherein the immunodeficiency is Selective IgA deficiency.

140. (Once Amended) A method of treating an immunodeficiency comprising administering to an individual, a therapeutically effective amount of a protein comprising a first amino acid sequence which is 90% or more identical to a second amino acid sequence consisting of amino acid residues 134-285 of SEQ ID NO:2, wherein the polypeptide having said first amino acid sequence modulates lymphocyte proliferation, differentiation, or survival.

141. (New) The method of claim 140 wherein the protein comprises a first amino acid sequence which is 95% or more identical to said second amino acid sequence.

142. (Once Amended) The method of claim 140 wherein the protein also comprises a heterologous amino acid sequence.

143. (New) The method of claim 142 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

144. (Once Amended) The method of claim 140 wherein said protein is labeled.

147. (Once Amended) The method of claim 140 wherein the immunodeficiency is common variable immunodeficiency (CVID).

149. (Once Amended) The method of claim 140 wherein the immunodeficiency is Selective IgA deficiency.

212. (Once Amended) A method of stimulating leukocyte proliferation, differentiation or survival comprising administering to an individual, a therapeutically effective amount of a protein comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;

(b) the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and

(c) the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

wherein the polypeptide having said amino acid sequence modulates lymphocyte proliferation, differentiation, or survival.

213. (New) The method of claim 212 wherein the protein comprises amino acid sequence (a).

214. (New) The method of claim 212 wherein the protein comprises amino acid sequence (b).

215. (New) The method of claim 212 wherein the protein comprises amino acid sequence (c).

216. (New) The method of claim 212 wherein the protein also comprises a heterologous amino acid sequence.

217. (New) The method of claim 216 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

218. (New) The method of claim 212 wherein said protein is labeled.

221. (Once Amended) A method of stimulating leukocyte proliferation, differentiation or survival comprising administering to an individual, a therapeutically effective amount of a protein comprising a first amino acid sequence that is 95% or more identical to a second amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;

(b) the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and

(c) the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

wherein the polypeptide having said first amino acid sequence modulates lymphocyte proliferation, differentiation, or survival.

222. (New) The method of claim 221 wherein the protein comprises amino acid sequence (a).

223. (New) The method of claim 221 wherein the protein comprises amino acid sequence (b).

224. (New) The method of claim 221 wherein the protein comprises amino acid sequence (c).

225. (New) The method of claim 221 wherein the protein also comprises a heterologous amino acid sequence.

226. (Once Amended) The method of claim 225 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

227. (New) The method of claim 221 wherein said protein is labeled.

230. (Once Amended) A method of stimulating leukocyte proliferation, differentiation or survival comprising administering to an individual, a therapeutically effective amount of a protein consisting of an amino acid sequence of amino acid residues 134-285 of SEQ ID NO:2.

231. (New) The method of claim 230 wherein the protein is fused to a heterologous amino acid sequence.

232. (New) The method of claim 231 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

233. (Once Amended) The method of claim 230 wherein said protein is labeled.

236. (Once Amended) A method of enhancing host defenses against infection comprising administering to an individual, a therapeutically effective amount of a protein comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;

(b) the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274 -284; and

(c) the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

wherein the polypeptide having said amino acid sequence modulates lymphocyte proliferation, differentiation, or survival.

237. (New) The method of claim 236 wherein the protein comprises amino acid sequence (a).

238. (New) The method of claim 236 wherein the protein comprises amino acid sequence (b).

239. (New) The method of claim 236 wherein the protein comprises amino acid sequence (c).

240. (New) The method of claim 236 wherein the protein also comprises a heterologous amino acid sequence.

241. (New) The method of claim 240 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

242. (New) The method of claim 236 wherein said protein is labeled.

245. (New) The method of claim 236 wherein the infection is an acute infection.

246. (New) The method of claim 236 wherein the infection is a chronic infection.
247. (New) The method of claim 236 wherein the infection is a bacterial infection.
248. (New) The method of claim 236 wherein the infection is a viral infection.
249. (New) The method of claim 236 wherein the infection is a parasitic infection.
250. (Once Amended) A method of enhancing host defenses against infection comprising administering to an individual, a therapeutically effective amount of a protein comprising a first amino acid sequence that is 95% or more identical to a second amino acid sequence selected from the group consisting of:
- (a) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;
 - (b) the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of 274-284; and
 - (c) the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;
- wherein the polypeptide having said first amino acid sequence modulates lymphocyte proliferation, differentiation, or survival.
251. (New) The method of claim 250 wherein the protein comprises amino acid sequence (a).
252. (New) The method of claim 250 wherein the protein comprises amino acid sequence (b).
253. (New) The method of claim 250 wherein the protein comprises amino acid sequence (c).

254. (New) The method of claim 250 wherein the protein also comprises a heterologous amino acid sequence.

255. (New) The method of claim 254 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

256. (New) The method of claim 250 wherein said protein is labeled.

259. (New) The method of claim 250 wherein the infection is an acute infection.

260. (New) The method of claim 250 wherein the infection is a chronic infection.

261. (New) The method of claim 250 wherein the infection is a bacterial infection.

262. (New) The method of claim 250 wherein the infection is a viral infection.

263. (New) The method of claim 250 wherein the infection is a parasitic infection.

264. (New) A method of enhancing host defenses against infection comprising administering to an individual, a therapeutically effective amount of a protein consisting of an amino acid sequence of amino acid residues 134-285 of SEQ ID NO:2 .

265. (New) The method of claim 264 wherein the protein is fused to a heterologous amino acid sequence.

266. (New) The method of claim 264 wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

267. (New) The method of claim 264 wherein said protein is labeled.

270. (New) The method of claim 264 wherein the infection is an acute infection.

271. (New) The method of claim 264 wherein the infection is a chronic infection.
272. (New) The method of claim 264 wherein the infection is a bacterial infection.
273. (New) The method of claim 264 wherein the infection is a viral infection.
274. (New) The method of claim 264 wherein the infection is a parasitic infection.
275. (New) The method of claim 89 wherein the immunodeficiency is common variable immunodeficiency (CVID).
276. (New) The method of claim 89 wherein the immunodeficiency is Selective IgA deficiency.
277. (New) The method of claim 98 wherein the immunodeficiency is common variable immunodeficiency (CVID).
278. (New) The method of claim 98 wherein the immunodeficiency is Selective IgA deficiency.